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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,338	10/31/2003	Birgit Sehested Hansen	6443.500-US	2536

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EXAMINER	
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ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
08/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,338	HANSEN ET AL.	
	Examiner	Art Unit	
	Brian-Yong S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5-7,14,15 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *17* is/are allowed.

6)☒ Claim(s) *2,5-7,14 and 15* is/are rejected.

7)☐ Claim(s) _ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicant's filing of amendment/remarks on 06/25/2009. By the amendment, claim 17 has been amended.

2. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

3. Claims 2, 5-7, 14-15 and 17 are currently pending for prosecution on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2, 5-7 and 14-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed compounds *per se* or salts of the claimed compounds *per se*, does not reasonably provide enablement for solvates of the claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

1). <u>The nature of the invention, state and predictability of the art, and relative skill of those in the art</u>

The invention relates to the treatment disorder selected from the group consisting of obesity, diabetes and impaired glucose tolerance comprising administering a compound of Formula (III) recited in claim 2 or a pharmaceutically acceptable salt or solvate thereof.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicant's invention would generally be a physician with a M.D. degree and several years of experience.

Solvates are crystal forms of a compound that encompass solvent molecules in the structure. Although solvates of known pharmacologically active agents are known, one skilled the art can not predict which compounds will form solvates and which will not. Methodology for forming solvates differs from compound to compound and although general methods that are routinely attempted exist, it is unpredictable whether they will result in formation of a solvate of any specific compound.

Since solvates are essentially crystalline forms of compounds, and it is acknowledged that crystal forms of compounds are unpredictable in their formation, formation of solvates is also necessarily unpredictable. There is no way for one skilled in the art to know, *a priori*, if a hydrate or solvate of a given compound even exists. For example, Vippagunta (Adv. Drug Del. Rev., 2001, vol. 48, 2001, pp. 3-26) teaches that the main challenges in managing the phenomenon of multiple solid forms of a drug is the inability to predict the number of forms that can be expected in a given case (page 11, right column). Furthermore, Vippagunta flatly states on page 18, section 3.4 the following:

"Predicting the formation of solvates or hydrates of a compound...is complex and difficult."

Thus, the state of the prior art does not support the broad scope of the above claims.

2). The breadth of the claims

The claims comprise plethora of compounds that correspond to the generic formula recited in claim 2 and any pharmaceutically acceptable salt or solvate thereof. Preparation of all of the compounds of claim 2 and solvates thereof would fall outside what one skilled in the art would consider routine experimentation.

3). The amount of direction or guidance provided and the presence or absence of working examples

The current specification fails to provide an example of a solvate of the instantly claimed compounds or a procedure for forming one. No data corresponding to any physical characteristic of a solvate is present. There is no evidence that applicant has successfully prepared a solvate of any of the compounds encompassed by the claims.

There are no working examples where a solvate of a compound of the instant claims is formed or identified.

4). The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that solvates of the claimed compounds could be predictably formed as inferred in the claims and contemplated by the specification.

Genentech Inc. vs. Nova Nordisk states, "[A] patent is not a hunting license. It is not a reward for a search but a compensation for its successful conclusion and 'patent protection' is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" (42 USPQ 2d 1001, Fed. Circuit 1997).

To practice the invention of the instant claims requires undue experimentation. Due to the acknowledged unpredictability in the formation of crystal forms and lack of direction from Applicants regarding procedures for the formation of crystalline forms and solvates of the claimed compounds, preparing such would require undue experimentation. The amount of experimentation required in order to produce solvates of thousands of the claimed compounds is extremely large and determining the methodology of crystalline compound production and solvate production of the claimed compounds would require inventive effort and extensive experimental burden.

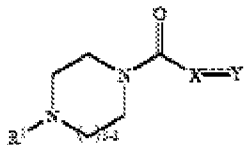
Accordingly, the instant claims do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 2, 5-7 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Dorwald et al. (US 7208497).

Dorwald discloses a compound of the general formula  such as 3-(3,5-di-tert-butyl-4-hydoxyphenyl)-1-(4-propyl-piperazin-1-yl)propenone or a pharmaceutically acceptable salt which reads on the instant formula III that is useful for the treatment of histamine H3 receptor mediated disease including obesity or impaired glucose tolerance, diabetes, especially Type 2 diabetes, etc... (column 23, lines 13-52; Example 23).

With respect to the recitation of "increasing mitochondrial respiration" in the claim 2, when the same compound is administered to treat the same patient population, the mechanism of action of "increasing mitochondrial respiration" deems to be inherent to the referenced method. Therefore, the reference anticipates the claimed invention.

With respect to the recitation of "a chemical uncoupler" in claim 14, such property or characteristic deems to be inherent to the referenced compound. Since the compound being a chemical uncoupler as defined is merely a characterization of the compound, Dorwald anticipates the claimed invention.

It is noted that the recitation of the compound having a slope calculated from an equation as defined in the instant claims is merely a characterization of the compound and therefore does not limit the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dorwald et al. (US 7208497).

The teaching of Dorwald has been discussed in above 35 USC 102(e) rejection. In addition, Dorwald teaches that aryl, namely phenyl, can be also substituted with one or more of cation containing substituents such as nitro, cyano, C1-6-alkylsulfonyl, etc… (column 8, line 60 through column 9, line 20; column 11, lines 33-67; column 12, lines 1-54).

Although Dorwald does not specifically mention the use of said compound in the form of "a cation", such determination of "cation" would have apparent to those skilled in the art under the meaning of 35 U.S.C. 103.

Response to Arguments

7. Applicant's arguments filed 06/25/09 have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that 3-(3,5-di-tert-butyl-4-hydoxyphenyl)-1-(4-propyl-piperazin-1-yl)propenone does not fall within the scope of the compounds encompassed by the genus recited in claim 2. Applicant alleges that R46 cannot encompass a piperazine-contatining structure, in view of the definitions of aryl and alkyl set forth on page 6 of the specifications as filed.

This argument is not found persuasive. Unlike the applicant's argument, it is generally recognized in the art that the term "aryl" includes both carbocyclic and heterocyclic ring (see column 3, lines 45-46 of US 5451596; column 3, lines 63-64 of US 5596020; column 3, lines 45-49 of US 5409930 and para. [0020] of US 20090176780 for your references). In other words, 3-(3,5-di-tert-butyl-4-hydoxyphenyl)-1-(4-propyl-piperazin-1-yl)propenone falls within "metes and bounds" of the claimed invention. Thus, the referenced compound clearly anticipates the instant invention.

The Patent and Trademark Office ("PTO") determines the scope of claims in patent applications not solely on the basis of the claim language, but upon giving claims their broadest reasonable construction "in light of the specification as it would be interpreted by one of ordinary

skill in the art." *In re Am. Acad. of Sci. Tech. Ctr.*, 367 F.3d 1359, 1364[, 70 USPQ2d 1827] (Fed. Cir. 2004). Indeed, the rules of the PTO require that application claims must "conform to the invention as set forth in the remainder of the specification and the terms and phrases used in the claims must find clear support or antecedent basis in the description so that the meaning of the terms in the claims may be ascertainable by reference to the description." 37 CFR 1.75(d)(1).

Applicant's argument in response to the examiner's rejection under 35 USC 103 is basically the same as discussed above, so the response discussed above applies here as well and is unpersuasive for reason just discussed

Conclusion

8. Claim 17 is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614